Remarks

Please cancel claims 60, 65, 68-69, 89-95 and 97. Please add new Claims 100-125. Claims 59, 61-64, 66-67, 79-88, 96 and 98-125 are in the case. Independent claims 59, 73, 96, 98 and 99 been amended to include the recitation of claim 60 that the anti-HIV ingredients consist of tenofovir disoproxil fumarate and emtricitabine. Claim 60 was indicated in the last office action to be allowable if placed in independent form. Claims 96, 98 and 100-125 are directed to the same subject matter with the further addition of the elected third agent Sustiva.

The examiner's attention is directed to copending USAN's Dahl et al. 11/453,122 and 11/452,472. A copy of the claims of these two applications are appended hereto for the examiner's convenience.

A supplemental IDS is supplied to bring the examiner's attention to a press release by the assignee of this application occurring about one month before the effective filing date of this application. Applicants supply a Form 1449 to facilitate the citation of this item to the record.

Applicants confirm their provisional election of the invention comprising tenofovir disoproxil fumarate (TDF), emtricitibine (FTC) and Sustiva, originally claims 59-93 and 96-99.

Claim 65 was objected to as being of improper dependent form. This issue should be moot as this claim has been cancelled.

Claims 59, 62-64, 66, 68-90, 92, 93 96, 98 and 99 were provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-8, 10, 15-20, 22-26, 42-55 and 58 of copending USAN 10/757,141. The '141 filing has been abandoned by express abandonment (a copy of letter of the abandonment is attached). This rejection should be moot.

Claims 59, 62-64, 66, 68-90, 92, 93, 96, 98 and 99 were rejected under 35 USC 103 as unpatentable over Chen et al. Chen et al. discloses treatment of HIV with an imidazole phosphonate anti-HIV compound. According to the examiner, claims that exclude the Chen et al. primary compound would be allowable, i.e., claims 60 and 61.

Accordingly, all of the independent claims herein have been amended to recite that the anti-HIV active ingredients consist of TDF and FTC, i.e., claim 60 has been incorporated into the independent claims.

By "anti-HIV active" ingredients applicants mean compounds that are therapeutically effective (FDA approved) when used alone for the treatment of HIV. According to applicants' understanding, the claims continue to include agents that might influence or modify the activity of such anti-HIV active ingredients even though the agents are not therapeutically effective against HIV in humans when used alone.

New claims 100-125 have been added that essentially replicate the 2-component pending set, but provide that the active drugs consist of TDF, FTC *and* Sustiva. These claims should be allowable for the same reason as noted in the previous paragraph.

The claims now should be in condition for allowance.

Respectfully submitted,

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App # 11/452,447

What is claimed:

1. A composition comprising dry granulated emtricitabine and tenofovir DF.

2. The composition of claim 1 wherein the water content (Karl Fischer) is about from 0.1 to 10% by weight.

3. The composition of claim 1 wherein the bulk density of the granules is about from 0.1 to 1 g/mL.

4. The composition of claim 1 wherein the geometric mean diameter of the granules is about from 50 to 800 micrometers.

5. The composition of claim 1 further comprising a pharmaceutically acceptable disintegrant.

6. The composition of claim 5 wherein the disintegrant is croscarmellose sodium or crospovidone.

7. The composition of claim 1 further comprising a pharmaceutically acceptable filler.

8. The composition of claim 1 further comprising a pharmaceutically acceptable binder.

9. The composition of claim 1 further comprising a pharmaceutically acceptable lubricant.

10. The composition of claim 1 as a unitary dosage form.

11. The composition of claim 10 which is a tablet.

12. The composition of claim 1 wherein the amount of emtricitabine and tenofovir DF is greater than about 70% by weight of the granules.

13. The composition of claim 12 wherein the amount of emtricitabine and tenofovir DF is about 77% by weight of the granules.

14. The composition of claim 1 which further comprises at least one pharmaceutically acceptable excipient.

15. The composition of claim 1 comprising (by approximate weight percent) emtricitabine 30.6, tenofovir DF 46.0, microcrystalline cellulose 13.7, croscarmelose sodium 7.3 and magnesium stearate 2.2.

16. The composition of claim 1 wherein the LOD is about 10%.

17. A method comprising granulating a composition comprising emtricitabine and tenofovir DF without contacting the composition with a destabilizing amount of liquid water.

18. The method of claim 17 wherein liquid water is not combined with the composition prior to or during granulation.

19. The method of claim 17 wherein the composition further comprises at least one pharmaceutically acceptable excipient.

20. The method of claim 17 wherein granulation comprises aggregating the composition and comminuting it to desired dimensions.

21. The method of claim 20 wherein the aggregation is accomplished by slugging or roller compaction.

22. The method of claim 20 wherein the composition is sieved to recover granules of the desired dimensions.

23. The method of claim 22 wherein the granules are retained by a 1.25 mm mesh.

24. The method of claim 19 wherein the excipient is a lubricant.

25. The method of claim 24 wherein the lubricant is an alkali metal salt of a C8-C18 fatty acid.

26. A unitary dosage form made by a process comprising dry granulation of a composition comprising emtricitabine and tenofovir DF.

27. A composition comprising greater than about 75% by weight emtricitabine and tenofovir DF.

28. A composition comprising granules comprising tenofovir DF, emtricitabine and croscarmellose sodium in an extragranular matrix also comprising croscarmellose sodium.

29. A method for antiviral therapy comprising administering an antivirally effective amount of the composition of claim 1 to a patient in need of antiviral therapy.

30. The method of claim 29 wherein the antiviral therapy is anti-HIV therapy.

App.# 11/453,122

What is Claimed:

1. A composition comprising tenofovir DF and a surfactant whereby the surfactant is in a stabilizing configuration with the tenofovir DF.

2. The composition of claim 1 additionally including efavirenz and emtricitabine.

3. The composition of claim 2 wherein the tenofovir DF and emtricitabine are in a first component and the efavirenz and the surfactant are in a second component.

4. The composition of claim 3 wherein the first component and the second component are physically discrete but are in contact with one another.

5. The composition of claim 4 wherein the components are layers.

6. The composition of claim 5 which is suitable for oral administration.

7. The composition of claim 5 which is a bilayer tablet weighing less than about 2.5 grams.

8. The composition of claim 3 wherein component 2 is produced by high shear wet granulation.

9 The composition of claim 1 wherein the detergent is sodium lauryl sulfate.

10. The composition of claim 3 wherein component 1 is produced by

dry granulation.

11. The composition of claim 2 wherein the total amount of efavirenz, emtricitabine and tenofovir DF is greater than about 60% by weight of the composition.

12. The composition of claim 2 which further comprises magnesium stearate, croscarmellose sodium, microcrystalline cellulose and hydroxypropyl cellulose.

13. The composition of claim 12 wherein the approximate percentages by weight of efavirenz, tenofovir DF, emtricitabine, magnesium stearate, croscarmellose sodium, microcrystalline cellulose, sodium lauryl sulfate, and hydroxypropyl cellulose are, respectively, about 39, about 19, about 13, about 2, about 7, about 17, about 1 and about 2.

14. The composition of claim 2 wherein efavirenz, emtricitabine and tenofovir DF are provided to a patient upon oral administration at substantially the same AUC and Cmax as the FDA approved products Truvada and Sustiva.

15. The composition of claim 7 which weighs about from 1200 mg to 2300 mg (including any film coating that is optionally present).

16. The composition of claim 7 wherein the layers are oriented horizontally along an axis of the tablet.

17. A container comprising the composition of claim 1 and a desiccant.

18. A method comprising preparing component 1 comprising tenofovir DF, preparing component 2 comprising efavirenz and a surfactant, and placing both components into stabilizing configuration with one another.

19. The method of claim 18 wherein component 1 also comprises emtricitabine.

20. The method of claim 19 wherein component 1 is made by dry granulation and component 2 is made by wet granulation.

21. The method of claim 20 wherein dry granulated tenofovir DF and emtricitabine are combined with magnesium stearate, wet granulated efavirenz is combined with magnesium stearate and the two magnesium stearate compositions compressed into a bilayer tablet.

22. A method comprising orally administering the dosage form of claim 1 to a patient in need of antiviral therapy.

23. The method of claim 22 wherein the dosage form is administered only once daily.

24. The method of claim 23 wherein the antiviral therapy is anti-HIV therapy.

25. A product comprising emtricitabine, tenofovir DF and efavirenz, a surfactant, and a means for preventing destabilizing contact between the surfactant and tenofovir DF.

26. A composition comprising emtricitabine, tenofovir DF and efavirenz which is free of pharmaceutically unacceptable concentrations of FTU,

mono-POC PMPA, dimer and mixed dimer.

27. The composition of claim 26 wherein the concentrations of FTU, mono-POC PMPA, dimer and mixed dimer are, respectively by weight %, 3.9, 9, 1.6, and 1.8.

28. The composition of claim 27 wherein the concentrations are determined after storage of the composition at 25°C/60% RH for 24 months.

29. A unitary dosage form comprising component 1 comprising tenofovir DF, and emtricitabine and component 2 comprising efavirenz and a surfactant, component 1 being spatially disposed in stabilizing configuration with component 2.

30. The dosage form of claim 29 which is suitable for oral administration.